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Primary Soft Tissue Non-Hodgkin Lymphoma in an AIDS Patient Successfully Treated with Chemotherapy Plus HAART

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Abstract

About 70% of AIDS-associated lymphomas are Non-Hodgkin lymphomas (NHL). Primary soft tissue NHL is very rare and accounts only the 0.1% of the cases. Generally, NHL of the soft tissue presents as large subcutaneous masses as primary clinical manifestation of neoplasm disease. Initially the mass lesions have a fast growing, with or without evidence of nodal or skin involvement. Here, we describe a patient with AIDS who developed a primary NHL of the soft tissue, presenting as a large subaxillary thoracic mass. Patient was successfully treated with highly active antiretroviral therapy plus chemotherapy with a prolonged survival and immune reconstitution.

Keywords: Non-Hodgkin Lymphoma; Soft tissue; HIV; AIDS

Abbreviations: NHL: Non-Hodgkin Lymphomas; HIV: Human Immunodeficiency Virus; BL: Burkitt´S Lymphoma; PBL: Plasmablastic Lymphoma; HAART: Highly Active Antiretroviral Therapy; CT: Computerized Tomography; WHO: World Health Organization; AIDS: Acquired Immune Deficiency Syndrome.

Introduction

Patients infected with human immunodeficiency virus (HIV) are at high risk to develop Non-Hodgkin lymphomas (NHL). The risk of NHL is 100 to 300-fold higher in HIV infected patients in comparison with the general population, being this second most frequent malignancy following Kaposi´s sarcoma. Generally, AIDS-associated NHL are a high grade lymphomas including diffuse large B cell lymphoma (DLBCL), Burkitt´s lymphoma (BL) and plasmablastic lymphoma (PBL), as most frequent subtypes and which are considered as an AIDS-defining illnesses. These patients are associated with a rapid progression of neoplasm disease, frequent extranodal initial manifestations, poor prognosis and a short survival after diagnosis [1-4]. Here we describe a case of primitive NHL of the soft tissue as primary manifestation of AIDS. We report the clinical characteristics, the diagnosis methods and the prolonged survival and immune reconstitution after highly active antiretroviral therapy (HAART) plus chemotherapy.

Case Report

A-26-year old man was admitted to the Infectious Diseases FJ Muñiz reference Hospital of Buenos Aires, because he present a two months history of fever, weight loss and night sweets. Physical examination revealed a large tumor lesion located on the chest wall in the right subaxillary region which extended to the subscapular zone (Figure 1). Tumor lesion had a hard consistency with adhesion to the deep tissues and with discreet changes on the overlying skin (Figure 2). A rapid test to HIV was positive and two 4° generation ELISA were also positive confirming the diagnosis of HIV infection. Significant laboratory findings include hematocrit 37%; hemoglobin 11.6 g%; erythrocyte sedimentation rate > 100 mm 1st h; white blood cells 4 300/mm^3; platelets 493 000/mm^3; lactate dehydrogenase of 2117 U/L. Renal and liver function were normal.

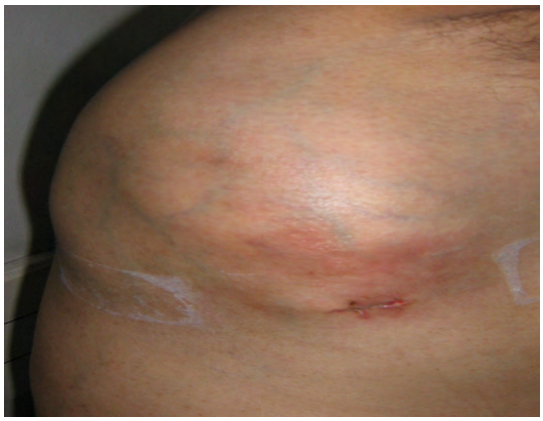

Figure 1: A large mass involving soft tissues on the chest wall in the right subaxillary region.

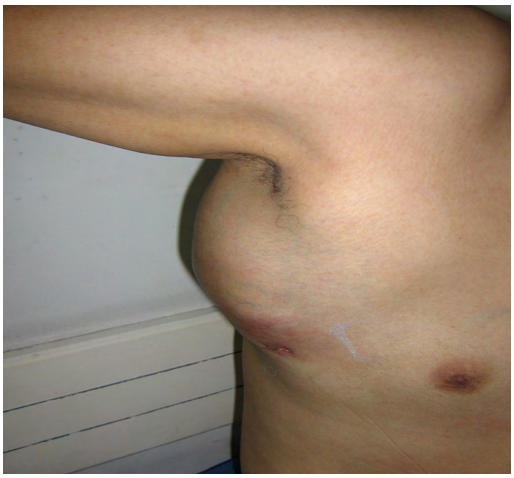

Figure 2: A subcutaneous tumor located on the chest wall without compromise of the skin or axillary lymphadenopathy.

The CD4-T-lymphocyte count was 85 cells/μL and the plasma viral load was up to 4.0 log_{10}. A thorax computed tomography (CT) scan was performed and revealed a large tumor lesion with hypodense areas of necrosis located on the right subaxillary region with extension to the subscapular homolateral region (Figure 3). Adjacent lymph nodes in relation to the axillary area were also seen. A CT scan of abdomen and pelvis showed a splenomegaly with a large hypodense heterogeneous mass that compressed the gastric chamber. A retroperitoneal ganglionic conglomerate was also detected. A surgical biopsy of the large soft tissue mass was performed. Histopathological examination with hematoxylin-eosin stain revealed a fibroadipose tissue with a dense proliferation of atypical lymphoid cells, with hyperchromatic and irregular nuclei, a poor cytoplasm and extensive areas of necrosis (Figures 4 and 5).

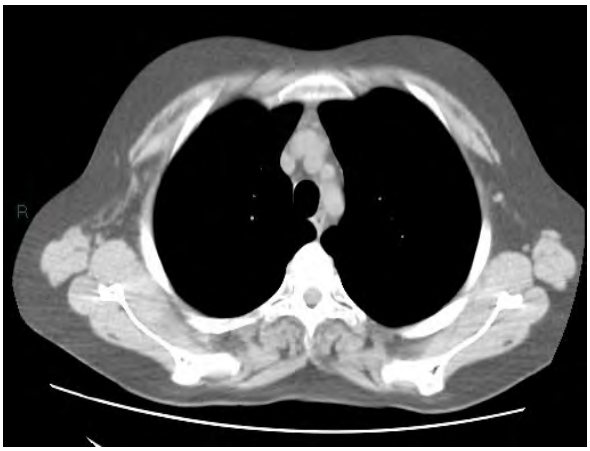

Figure 3: H/E 100x: showed a dense proliferation of atypical lymphoid cells, with hyperchromatic and irregular nuclei.

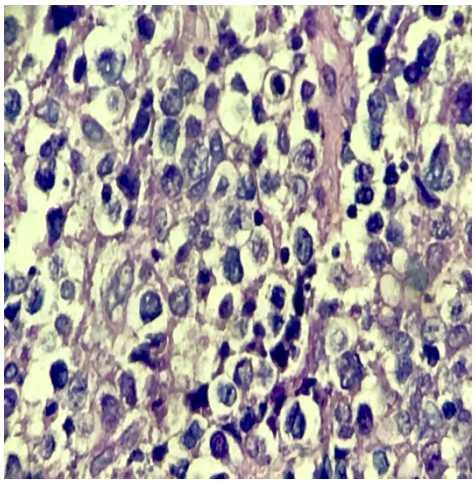

Figure 4

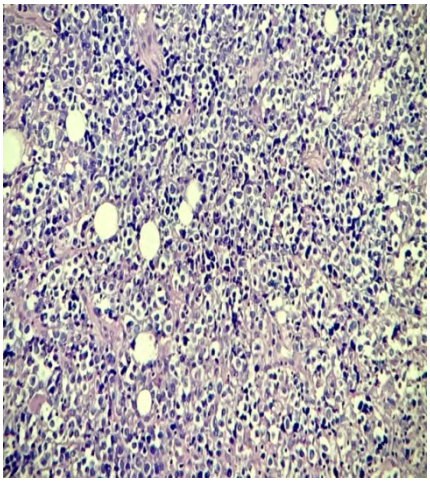

Figure 5

Figures 4 and 5: H/E 200x: revealed the existence of an atypical and dense infiltrate, relativity uniform, composed of medium and large cells with a moderate or poor cytoplasm, an eccentric and irregular nuclei, and one or more large nucleoli.

Immunohistochemical stains were applied; the neoplastic cells were positive and expressed CD20 (B-phenotype), CD45, CD10 and BCL6 (centrogerminal phenotype) and were negative for CD3. A 10% of the atypical cells co-expressed BCL2 and less than 10% were MUM1 positive. Ki67 proliferation index was 95%. According to the criteria of the World Health Organization (WHO) and based of the histopathological morphology and the cell immunophenotype, final diagnosis was a primary soft tissue DLBCL [5]. A bone marrow biopsy was performed without infiltration by atypical lymphoid cells. Ann Arbor clinical classification was IIIB [6]. Patient was started on HAART based on tenofovir, emtricitabine and efavirenz and initiated a chemotherapy scheme of 6 cycles including cyclophosphamide, vincristine, liposomal doxorubicin, etoposide, meprednisone, granulocyte colony stimulating factor and the monoclonal antibody anti-CD20 rituximab (R-DAEPOCH). The first cycle was done with 50% of the doses because the patient presented less than 100 CD4 T-cell/μL. After the 6th cycle of chemotherapy and with a good tolerance and adherence to HAART patient presented a total remission of the lymphoproliferative disease. Two years after, he keep going in a good clinical condition, with undetectable plasma viral load and a CD4 T-cell count of 445 cell/μL.

Discussion

NHL represents a heterogeneous group of malignancies generally originated in the lymphoid tissue of the lymph nodes. Frequently, this neoplasm spread and involves other organs[5]. In the general population, NHL is approximately eight times more common in comparison with Hodgkin's disease. Also, extranodal involvement is much more frequent in NHL, especially in HIV population. One of the most common characteristics of AIDS-associated NHL is the extranodal compromise as the first clinical manifestation of the disease. Extensive local invasion and rapid disseminated disease are two other frequent findings of HIV-associated NHL [5,6]. Additionally, some patients present with "B" symptoms (prolonged fever, night sweats and weight loss), similar to frequent opportunistic infections in AIDS patients as tuberculosis, atypical mycobacteriosis, visceral leishmaniosis and histoplasmosis. The incidence of NHL among patients infected with HIV has been estimated from 5% to 20%. After the widespread of HAART, a reduction of primary central nervous lymphoma has been observed. However, the incidence of other subtypes of lymphomas remains invariable [7,8]. Soft tissues involvement is rare in NHL and is described only in 0,1% of the cases[4].

Primary NHL of the soft tissue was defined as those lymphomas presenting with involvement of the soft tissue or the muscle as the predominant manifestation of the disease[9]. Generally, NHL of the soft tissue presents as large subcutaneous masses, as we could see in this patient. The most common site of involvement is the chest wall. Soft tissue lymphomas include those masses that involve the subcutaneous and the musculoskeletal tissues; in our experience, these neoplasms are characterized by his fast growth with the frequent involvement of the adjacent tissues as the skin and the bone. Regional nodal infiltration is also frequent [9,10]. Salamao et al [11] published a clinic pathologic study of a large series that include 19 patients who developed lymphomas of the soft tissue as large masses without evidence of lymph node involvement. The sites of involvement include low and upper chest wall, gluteal and frontal regions. Histological and immunophenotype studies revealed twelve large lymphomas, two small non-cleaved lymphomas (B-cell phenotype) and five low grade B cell lymphomas. The authors conclude that malignant lymphomas initially diagnosed in the soft tissues are most commonly large cell lymphomas with a B-cell phenotype, as in the patient we describe. In our experience, ultrasound of the muskuloskeletal tissue has an important role in the diagnosis of these malignant tumors, especially to define the extent and the relationship of the mass with the surrounding structures.

Additionally, it can be used in fine needle guided aspiration biopsy to obtain a sample for tissue diagnosis. Treatment of HIV-associated NHL includes the combination of HAART plus chemotherapy. Treatment regimens include CHOP (cyclophosphamide, doxorubicin, vincristine and

prednisone) or CHOP-like regimens. In some studies [12-15], the addition of HAART to the chemotherapy has had a favorably impact on the survival of HIV-associated NHL, as we can see in our patient. In conclusion, we think that NHL should be included in the differential diagnosis of soft tissue masses in HIV-seropositive patients. Early excision biopsy is necessary to confirm the diagnosis of these neoplasms and to determine the histopathological subtype. Early diagnosis followed by chemotherapy plus HAART is necessary to achieve a good clinical outcome in this kind of patients.

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